REMARKS

Claim 23 is pending in the present application. Claim 23 was rejected under 35 U.S.C. §112, first paragraph and second paragraph.

The specification has been amended to correct the spelling of the word "aptamer", which was previously misspelled due to a typographical error.

New claims 24-49 have been added herein without prejudice or disclaimer of any previously claimed subject matter.

Support for new claims may be found in the specification generally in Example VI and more specifically as follows: Support for claim 24 may be found in the specification for example on page 63, lines 17-23, and on page 64, lines 3-26. Support for claims 25-27 may be found for example on p. 57, lines 8-10. Support for claim 28 may be found for example on p. 62, line 7. Support for claims 29 and 31 may be found for example on p. 71, lines 17-19. Support for claim 30 may be found for example in Figure 31 and on page 13, line 6. Support for claim 32 may be found for example on p. 57, lines 31-32. Support for claim 33 may be found for example on p. 71, lines 5-7. Support for claim 34 may be found for example on p. 62, line 32 - p. 63, lines 1-2. Support for claim 35 may be found for example on p. 67, lines 5-15. Support for claim 36 may be found for example on p. 69, lines 12-16. Support for claim 37 may be found for example on p. 62, lines 26-28. Support for claim 38 may be found for example on p. 63, lines 21-23. Support for claims 39-40 may be found for example on p. 62, lines 1-2. Support for claim 41 may be found for example on p. 63, lines 22-24. Support for claims 42 and 43 may be found for example on p. 64, lines 4-6. Support for claim 44 may be found for example on p. 57, lines 12-20. Support for claim 45 may be found for example on p. 61, lines 26-28. Support for claims 46 and 47 may be found for example on p. 63, lines 3-13. Support for claim 48 may be found for

example on p. 65, line 22. Support for claim 49 may be found for example on p. 68, lines 14-20. Thus, no new matter has been added by the foregoing amendments.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is entitled "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**".

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover has not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants acknowledge with appreciation withdrawal of the previous rejections under 35 U.S.C. §102.

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Entry of this Amendment is respectfully requested.

Rejection under 35 U.S.C. §112, second paragraph

Claim 23 is newly rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleges that the metes and bounds of the structure of the target molecule, the catalytic RNA (inactive and active states) and the substrate are not clear from the claim as written and that it is not clear from the specification as filed that

the structure of the claimed invention is such that one skilled in the art has a clear idea of the steps involved. Applicants respectfully traverse this rejection.

The structure of the target molecule, the catalytic RNA (inactive and active states) and the substrate are described in the specification, *inter alia*, generally in Example VI, pages 56-71. This example describes ways in which binding of a catalytically inactive RNA molecule to a target molecule can stabilize the RNA molecule in a form in which it is catalytically active towards a substrate other than the target molecule. Catalytic activity towards the substrate indicates presence of the target, since binding of the RNA to the target is necessary for catalysis.

The specification provides examples of the structures of the claimed invention such that one skilled in the art would have a clear idea of the steps involved in practicing the invention. Examples of target molecules are provided in the specification. For example, the target molecule may be a polynucleotide (see, for example, p. 57, lines 8-10), a polypeptide , a small molecule, or a metal ion (see, for example, p. 71, lines 17-19). Binding of a catalytically inactive RNA molecule to a target molecule may stabilize the RNA in its catalytically active form (see, for example, p. 71, lines 6-8). Examples of catalytically active RNA structures are well known to those skilled in the art, and include both hairpin and hammerhead ribozymes (see, for example, p. 57, lines 31-32 and p. 71, lines 5-7). Examples of reactions catalyzed by the RNA in its catalytically active form include cleavage or ligation of substrates other than the target to which the RNA is bound (see for example, p. 57, lines 31-32, and p. 61, lines 31-32). Examples of substrates other than the target molecule are described in the specification and include polynucleotides such as capture probes and replicase probes (see, for example, p. 64, lines 22-26, p. 57, lines 11-20, and Figure 26).

Thus, Applicants believe that these claims distinctly claim the subject matter which Applicants regard as their invention and that a skilled artisan would have a clear idea of the steps involved in practicing Applicants' invention from the specification as filed. Accordingly,

Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph..

Rejection of Claim 23 under 35 U.S.C. §112, first paragraph

Claim 23 stands rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The examiner also alleges that in view of the 35 U.S.C. § 112, second paragraph, rejection above, it is not clear what the metes and bounds of the structure of the claimed invention is, and thus it is not enabled for one skilled in the art to make and use the invention as claimed.

Applicants respectfully traverse this rejection and submit that the metes and bounds of the structure of the claimed invention are described in Example VI of the specification (p. 56, line 19 - p. 71, line 24), entitled "Target-Activated RNA Catalysis for Nucleic Acid Detection" and in Figures 25, 26, 27, 28, 29, 31, and 32. In particular, use of a capture probe is described, for example on p. 63, lines 22 - 24. Where the target comprises, for example, RNA, the capture probe may comprise both sequences that are complementary to the target and sequences that may serve as the substrate for a catalytically active RNA, allowing hybridization between the capture probe and the target (p. 63, lines 18-23; Figure 26) and also allowing the capture probe to serve as the substrate for a catalytically active RNA. In addition to hybridization between the capture probe and the target, a catalytically inactive RNA molecule, which contains sequences complementary to the target molecule (p. 64, lines 18-19), may also hybridize with the target. The catalytically inactive RNA becomes active upon binding to the target, catalyzing cleavage of the substrate sequence of the bound capture probe (p. 64, lines 22-26). The catalytic RNA may be, for example, a hairpin ribozyme (p. 57, lines 31-32) or a hammerhead ribozyme (p. 71, lines 5-7). In addition to the endonuclease cleavage reaction described for catalysis towards a capture

probe, the catalytic RNA may also catalyze a ligation reaction (p. 57, lines 31-32). Target-dependent ligation of replication probes by the catalytic RNA, followed by amplification of the ligation product by Qβ replicase, is described (p. 57, lines 11-20; p. 65, lines 19-22), allowing for detection of the target molecule by, for example, the presence of a fluorophore such as ethidium bromide (p. 68, lines 14-17).

In view of the foregoing, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants have, by way of the amendments and remarks presented herein, made a sincere effort to overcome rejections and address all issues that were raised in the outstanding Office Action. Accordingly, reconsideration and allowance of the pending claims are respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 367592000100. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: August 14, 2001

By: Jill A. Jacobson

Jill A. Jacobson
Registration No. 40,030

Morrison & Foerster LLP
755 Page Mill Road
Palo Alto, California 94304-1018
Telephone: (650) 813-5876
Facsimile: (650) 494-0792

OIPE JC54
AUG 14 2001
PATENT & TRADEMARK OFFICE

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification

The paragraph beginning at p. 13, line 3, has been amended as follows:

Fig. 31. Scheme for Using Hammerhead Ribozymes to Detect any Molecule.
Fig. 31 presents a scheme for using a hammerhead ribozyme to detect the presence of any molecule (filled oval), which upon encountering the probe, assembles an [optomer] aptamer from dangling ends to which it specifically binds, thereby stabilizing the active conformation of a ribozyme. Subsequent cleavage detected by any of several techniques such as release of biotin from a solid support.